Exhibit R-2, PB 2010 Defense Advanced Research Projects Agency RDT&E Budget Item Justification									DATE: May 2009	
APPROPRIATION/BUDGET ACTIVITY 0400 - Research, Development, Test & Evaluation, Defense-Wide/BA 2 - Applied Research					R-1 ITEM NOMENCLATURE PE 0602383E BIOLOGICAL WARFARE DEFENSE					
COST ($ in Millions)	**FY 2008 Actual**	**FY 2009 Estimate**	**FY 2010 Estimate**	**FY 2011 Estimate**	**FY 2012 Estimate**	**FY 2013 Estimate**	**FY 2014 Estimate**	**FY 2015 Estimate**	**Cost To Complete**	**Total Cost**
Total Program Element	64.127	56.139	40.587						Continuing	Continuing
BW-01: BIOLOGICAL WARFARE DEFENSE	64.127	56.139	40.587						Continuing	Continuing

A. Mission Description and Budget Item Justification

(U) DARPA's Biological Warfare Defense project is budgeted in the Applied Research Budget Activity because its focus is on the underlying technologies associated with pathogen detection, prevention, treatment and remediation. This project funds programs supporting revolutionary new approaches to biological warfare (BW) defense and is synergistic with efforts of other Government organizations.

(U) Efforts to counter the BW threat include countermeasures to stop pathophysiologic consequences of biological or chemical attack, host immune response enhancers, medical diagnostics for the most virulent pathogens and their molecular mechanisms, tactical and strategic biological and chemical sensors, advanced decontamination and neutralization techniques, and integrated defensive systems. This program also includes development of a unique set of platform technologies that will dramatically decrease the timeline from military threat detection to countermeasure availability.

B. Program Change Summary ($ in Millions)

	FY 2008	FY 2009	FY 2010	FY 2011
Previous President's Budget	72.101	66.291	55.398	
Current BES/President's Budget	64.127	56.139	40.587	
Total Adjustments	-7.974	-10.152	-14.811	
Congressional Program Reductions	0.000	-10.152		
Congressional Rescissions	-6.000	0.000		
Total Congressional Increases	0.000	0.000		
Total Reprogrammings	0.000	0.000		
SBIR/STTR Transfer	-1.974	0.000		
TotalOtherAdjustments			-14.811	

Change Summary Explanation

FY 2008

Decrease reflects Section 8042 rescission and the SBIR/STTR transfer.

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FY 2009
Decrease reflects the reduction for Section 8101 Economic Assumptions and a program element execution adjustment.

FY 2010
Decrease reflects draw down of biological warfare defense (BWD) efforts as programs transition directly to elements of the DoD (i.e., the Army, Defense Threat Reduction Agency) that have cognizance over Service BWD materials and systems, and reclassification of sensor development programs to protect the technological attributes of the systems.

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COST ($ in Millions)	**FY 2008 Actual**	**FY 2009 Estimate**	**FY 2010 Estimate**	**FY 2011 Estimate**	**FY 2012 Estimate**	**FY 2013 Estimate**	**FY 2014 Estimate**	**FY 2015 Estimate**	**Cost To Complete**	**Total Cost**
BW-01: BIOLOGICAL WARFARE DEFENSE	64.127	56.139	40.587						Continuing	Continuing

A. Mission Description and Budget Item Justification

(U) DARPA's Biological Warfare Defense project is budgeted in the Applied Research Budget Activity because its focus is on the underlying technologies associated with pathogen detection, prevention, treatment and remediation. This project funds programs supporting revolutionary new approaches to biological warfare (BW) defense and is synergistic with efforts of other Government organizations.

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
Unconventional Therapeutics	26.235	20.470	22.950	
(U) This thrust is developing unique and unconventional approaches to ensure that soldiers are protected against a wide variety of naturally occurring, indigenous or engineered threats. Past successes in this effort have come from developing therapeutics that are designed to work against broad classes of pathogens. This has led to several significant transitions, a separate thrust in Anthrax countermeasures, and most recently a program at Defense Threat Reduction Agency (DTRA) that directly capitalizes on previous DARPA investments. Work in this area has also uncovered new approaches to therapeutics that, rather than attacking specific pathogens, enhance innate human immune mechanisms against broad classes of pathogens. Integral to these efforts is the development of methods that rapidly identify a broad spectrum of pathogens. Not only will these approaches be more effective against known pathogens, they also promise to offer substantial protection against unknown pathogens including engineered and emerging pathogens from third-world environments.				

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
(U) A current emphasis is on the discovery and development of technologies that will allow a rapid response (within weeks) to unanticipated threats, whether they are naturally encountered emerging diseases or agents from intentional attack. This thrust has a goal of radically transforming the protein design process by researching and developing new mathematical and biochemical approaches to the in silico design of proteins with specific functions. This program is also developing an interactive and functional in vitro human immune system using tissue engineering. This "immune system" will be able to test the efficacy of vaccines against threat agents that, at the present time, can only be tested in animal models. This significantly decreases the time needed and increases the probability of success for biological warfare vaccine development. An additional focus is the development of entirely new technologies that will allow the rapid, cost-effective manufacture of complex therapeutic proteins such as monoclonal antibodies and vaccine antigens; these technologies will reduce the time for biologics manufacture from years (or even decades) to only weeks. *FY 2008 Accomplishments:* - Demonstrated plant and bacteria platform with more than 1000-fold increase in vaccine protein manufacturing rate using performer-chosen agent. - Demonstrated fungus platform with a 10-fold increase in monoclonal protein manufacturing rate. - Expressed multiple monoclonal antibodies (mAbs) using 7 strains of new mushroom-specific condon algorithms. - Produced over one million pounds of biomass in 6.5 weeks and developed enhanced purification method for downstream processing. - Predicted historical failed therapeutics using only the artificial human immune system. - Demonstrated government and commercial collaboration by using the artificial human immune system to test vaccine candidates for human response. - Demonstrated fusogenic properties of antibodies. - Developed approaches for on-site battlefield synthesis of small molecule therapeutics, including antibiotics. - Merged molecular imprinting with organic nanoparticles to generate functional viral replicates.				

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B. Accomplishments/Planned Program ($ in Millions)		**FY 2008**	**FY 2009**	**FY 2010**	**FY 2011**

FY 2009 Plans:

- Express two DARPA-specified challenges to demonstrate flexibility of platform; one of which is in accordance with Food and Drug Administration (FDA) current good manufacturing processes (cGMP).
- Demonstrate plant platform capability to produce three million doses of DARPA-specified vaccines in twelve weeks with improved biochemistry metrics.
- Demonstrate fungus platform capability to produce three million doses of DARPA-specified monoclonals in twelve weeks with improved biochemistry metrics to provide confidence prior to entering FDA trials.
- Demonstrate mushroom platform capability to produce three million doses of DARPA-specified vaccine and/or monoclonals in twelve weeks with improved biochemistry metrics to provide confidence prior to entering FDA trials.
- Demonstrate improved biochemistry metrics which include: protein solubility (greater than ninety-nine percent), fragmentation (less than 0.1 percent) and folding (greater than 99.9 percent) for both vaccine and monoclonal platforms. These are over and above the current FDA best of class, to provide confidence prior to entering FDA trials.
- Demonstrate pathway to reduction of vaccine and/or monoclonal production cost per dose.
- Ensure thirty percent mass efficiency from base components to final medication, and a flow-through rate of forty-five standard doses per hour of one medication and five standard doses per hour of each of the seven medications.
- Create a controlled environment to monitor pathogen evolution in response to host specific interactions including vaccination.

FY 2010 Plans:

- Complete demonstration of 100-fold increase in manufacturing rate. Performers that are creating a vaccine platform will need to show a manufacturing rate greater than or equal to 100 doses per liter times number of weeks. Those that are developing a monoclonal platform technology must demonstrate a manufacturing rate greater than or equal to 2.5 doses/per liter times number of weeks.
- Significantly reduce vaccine production costs to one dollar per dose and/or monoclonal production to ten dollars per dose.

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
- Demonstrate proof of scale-up and platform flexibility through a live fire test. Each performer will produce 1,000 doses of vaccine and/or monoclonal at lab-scale cGMP against a DARPA-designated unknown agent in twelve weeks, including final manufacturing rate, biochemistry and cost metrics. - Demonstrate dose efficacy using animal models and DARPA's Rapid Vaccine Assessment (RVA) artificial human immune system. - Document contaminants, system development, and quality control to facilitate pre-investigational new drug meetings with FDA. - Integrate diverse species specific host cell responses to pathogens within a microenvironment circuit model. - Refine resolution of metamaterial lenses to pathogenic scales. - Develop laser refractive mechanism and sample target control device. - Identify a unified, coherent global strategy for addressing all remaining gaps in the Nation's biodefense capability. - Identify means to prevent infection by hardening host against infection, weakening the pathogen and preventing secondary infection. - Develop approaches for preventing death by converting deadly to non-lethal pathogens. - Develop techniques for including transient immunity by transplanting immunity from survivors, rapidly creating neutralizers and re-targeting immunity.				
External Protection (U) This program is developing and demonstrating a variety of technologies to protect soldiers from the hazards of chemical, biological and radiological attack, and other hazards such as large unstable weapons stores. The program includes the autonomous detection and self-cleaning of surfaces contaminated by an attack, and the safe neutralization of hazardous materials. This program will focus on the integrated thermal model of combatant in operational conditions and address the heat transfer coupling for better evaporative cooling. *FY 2008 Accomplishments:* - Optimized active textile cells for improved gas generation efficiency, lifetime, sporacidal ability, and cell reliability.	1.500	4.848	1.000	

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B. Accomplishments/Planned Program ($ in Millions)		**FY 2008**	**FY 2009**	**FY 2010**	**FY 2011**
- Developed additives (surface active biocides, nutrients, microspheres) into a spray and spread coatable chemical agent resistant coating (CARC) resin to enhance biocidal effect at moderate humidity. - Developed atmospheric pressure cold plasma deposition processes to deposit biocidal materials that are 100 percent compatible with semiconductor devices and capable of killing spores. - Demonstrated process compatibility with high sensitivity electronic components and subsystems. - Demonstrated efficacy and durability after exposure to vaporous hydrogen peroxide, a currently planned active decontamination technique that complements the self-decontaminating surfaces capabilities. *FY 2009 Plans:* - Demonstrate biocidal efficacy of active textile cells on animal remains. - Field test the optimized self-decontaminating polyurethane based CARC on military vehicles at Dugway Proving Grounds using biological warfare simulants. *FY 2010 Plans:* - Develop an integrated thermal model of a combatant under operational conditions including bioheat generation, internal convective (blood) and conductive (tissue) heat transfer, and coupling to ambient heat baths by radiation, conduction, evaporation, and convection. - Investigate fabrics and garment architectures that allow tuning of evaporative and convective heat transfer from the body behind a chemically impermeable external shell.					
Advanced Diagnostics (U) In the early stages, many illnesses caused by biological warfare (BW) agents are either asymptomatic, or else have flu-like symptoms and are indistinguishable from non-BW related diseases. Early diagnosis is key to providing effective therapy. The Advanced Diagnostics program will develop the capability to detect the presence of infection by biological threat agents, differentiate them from other pathogens (including those of non-BW origin), and identify the pathogen even in the absence of recognizable clinical signs and symptoms (i.e., while the pathogen numbers are still low). Novel approaches including the use of breath and advanced mathematical analysis will be examined.		12.265	9.527	0.000	

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
FY 2008 Accomplishments: - Identified parameters that indicate presence of a viral infection before symptoms occur. - Developed algorithms that can predict illness from rhinovirus, respiratory syncytial virus and influenza B as well as other upper respiratory pathogens prior to onset of symptoms. - Identified candidate molecular markers to enable development of rapid diagnostic platform. - Developed preliminary model to describe host genomic response to rhino virus infection. - Continued to develop medical countermeasures that alleviate radiation exposure in experimental models. - Continued evaluation of non-invasive rapid biodosimeters that can be used to triage large populations in the event of a large radiological/nuclear event. - Completed evaluation of volatile organic compounds in the breath of explosive handlers. - Demonstrated Receiver Operating Curve (ROC) for detection of explosive handlers and bystanders. - Demonstrated reversible mechanical alterations in protein structure that yield a 2-fold change in affinity to biological, chemical and environmental agents. *FY 2009 Plans:* - Refine predictive model of impending illness to increase the probability of detection and reduce probability of false alarms. - Confirm predictive model of impending illness accuracy in large sample-size, warfighter relevant populations. - Evaluate potential diagnostic platforms for rapid identification of host molecular markers, which indicate viral infection prior to the onset of symptoms. - Develop proof of concept biosensors based on “best fit” of diagnostic platforms, predictive models, and host molecular marker studies. - Evaluate radiation technologies at the Armed Forces Radiobiology Research Institute (AFRRI) in a live fire test to identify best biodosimeters.				
Sensors (U) The Sensors program goal is to develop a unique set of biological warfare (BW) sensors that will greatly improve sensitivity and response time to bacteria, viruses and/or toxins.	11.627	10.000	16.637	

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
(U) The Hyperadsorptive Atmospheric Sampling Technology (HAST) program will develop systems that permit exhaustive, accurate, and economical collection of atmospheric trace constituents to support chemical mapping of urban and military environments. The system, which integrates three technical components, will demonstrate materials, packaging, and extraction technologies that sample atmospheric impurities whose concentration ranges from 20 parts per trillion to 200 parts per million by volume from 100 liter-atmospheres of gas in less than five minutes. New methods to swiftly and economically identify and characterize mixtures of trace gases to support chemical mapping and reconnaissance will also be developed. These new methods will enable identification of chemical compounds for which library spectra are unavailable. HAST will collect chemical samples that will be utilized to generate chemical maps that enable tactical chemical awareness, strategic intelligence, and force protection. *FY 2008 Accomplishments:* Hyperadsorptive Atmospheric Sampling Technology (HAST) - Developed new materials including metal organic framework structures and amorphous carbide-derived carbon lattices. - Initiated new manufacturing methods derived from embossed rolled films and compact discs. *FY 2009 Plans:* - Develop prototype instrument to identify sort mixtures of up to 100 gases. - Develop and test extraction methods. - Integrate new materials with optimal packaging approaches. - Measure probability of detection and probability of false positive for trace gas samples of hundreds of picomoles. *FY 2010 Plans:* - Optimize manufacturing technology at useful scales. - Develop technologies and algorithms to identify pure gases without the use of spectral libraries. - Extend analytical instrument sensitivity to tens of picomoles of up to 300 gases. - Increase rate of analysis to thousands of samples per day.				

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
- Develop protocol for identification of unknown gases in micromole quantities without library spectra. - Integrate fundamental spectroscopic and quantum chemical analyses to identify unknown gases.				
Threat Agent Cloud Tactical Intercept Countermeasure (TACTIC) (U) The Threat Agent Cloud Tactical Intercept and Countermeasures (TACTIC) program will develop and demonstrate the capability to 1) rapidly detect, classify and identify an airborne chemical warfare agent/ biological warfare agent (CWA/BWA) battlefield threat at stand-off distances, and 2) use countermeasures to neutralize and/or precipitate the threat before it reaches the intended target. The TACTIC program will develop a prototype system having an integrated approach for the classification/identification (CI) and countermeasure (CM) of aerosolized CWA/BWA threat clouds. The TACTIC system prototype will be evaluated in a controlled breeze tunnel testing environments with variations in range, concentration and wind speed. Upon successful completion of the preliminary design and critical design reviews, a prototype system will be built to demonstrate an effective CI and CM systems capability in open air tests. A memorandum of agreement (MOA) is in place with the Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) for transitioning this capability to the Army. *FY 2008 Accomplishments:* - Completed Conceptual Design Review. - Began bench scale, drop tube, and chamber testing of the CI/CM against CWA/BWA aerosolized threat clouds. - Began modeling threat scenarios by the independent validation and verification (IV and V) team. - Evaluated the performers' systems' technology readiness level (TRL) following each technical review. - Completed Preliminary Design Review (PDR). *FY 2009 Plans:* - Commence Critical Design Review (CDR). - Complete and validate models of CI/CM subsystem performance for operationally realistic tests.	10.000	8.430	0.000	
Mission-Adaptable Chemical Sensors (MACS)	2.000	2.864	0.000	

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B. Accomplishments/Planned Program ($ in Millions)	FY 2008	FY 2009	FY 2010	FY 2011
(U) At present, chemical sensors are unable to combine sensitivity (parts-per-trillion (ppt)) and selectivity (unambiguous identification of molecular species) with low false alarm rate. This effort will develop a sensor, based upon rotational spectroscopy of gases that will have superior capability in all categories; it will achieve the highest possible sensitivity in ppt for unambiguous detection of all chemical species. A preliminary blind test showed complete and unambiguous identification of an unknown sample containing multiple chemical species with a sampling time of one second and a false alarm probability below 0.001%. At present, the program has investigated the nature of the atmospheric background “clutter” at the parts per billion (ppb) level and below to enable the identification of target signatures at highest sensitivity. The program will focus on reduction of size and simplicity of function to achieve portability and simultaneous detection of a large number (hundreds) of species. The capabilities will far surpass all other current sensors. *FY 2008 Accomplishments:* - Constructed and demonstrated a fully-integrated, portable, prototype chemical sensor system able to identify more than 30 analytes correctly. *FY 2009 Plans:* - Identify users and particularize the MACS sensor for their objectives. - Extend the spectral reference library of analytes to hundreds to suit the different applications. - Automate the sensor to identify the chemical analytes within a sample using computer lookup. - Reduce sample analysis time to less than one minute.				
Biomedical Engineering Initiative *FY 2008 Accomplishments:* - Developed biosensors to identify blood-borne biomarkers of tissue trauma that convey information concerning injury severity and prognosis.	0.500	0.000	0.000	

C. Other Program Funding Summary ($ in Millions)

N/A

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D. Acquisition Strategy

N/A

E. Performance Metrics

Specific programmatic performance metrics are listed above in the program accomplishments and plans section.